

Reactions to Thioproperazine ("Majeptil")

SIR,—I was interested to read the memorandum by Drs. P. T. Annesley and A. K. Mant (January 27, p. 233) on a fatal reaction to thioproperazine.

In the spring and summer of 1961 I arranged to run a trial experiment with thioproperazine ("majeptil") and the manufacturers kindly supplied me with the medication necessary. I followed meticulously in this trial-run the method laid down by Denham and Carrick¹ and even had the help of one of the authors to reproduce optimal conditions. The trial was carefully charted, the method worked out by the nursing staff in foolproof detail, and the side-effects and their treatment were laid down most clearly. The neurological conditions were checked daily.

The patients were chosen from chronic deteriorated schizophrenics who had undergone most kinds of treatment, and every one of them had previously had prolonged courses of E.C.T., high dosage chlorpromazine therapy,² maintenance therapy on chlorpromazine, trifluoperazine, and orphenadrine.

In October and November I reported back to the manufacturers giving the following results:

Of 17 patients four had to be withdrawn during the first course because the side-effects were overstepping the limit of the borderline of what can or cannot be done to patients. Out of the remaining 13 nine had three full courses, one had four courses, three had five courses, going right up to 90 mg. t.d.s. The side-effects were very severe, but none of them were irreversible. Four of them became quite ill with gross physical emaciation and needed weeks of very careful nursing to get them back to the state they were in before starting the treatment. One man developed such uncontrollable hyperactivity after only two tablets of 5 mg. that he had to be secluded and was in need of the attention of three nurses for 72 hours. Another case developed an opisthotonos and oculogyric crisis, and in this case I was very worried as he was a young man of 24. Here too I interrupted the course at once. The same patient developed a duodenal ulcer three weeks after the interruption of the majeure trial, and though one cannot blame the medication I think that the enormous stress to which this man was exposed physically through the side-effects of the drug may have had a bearing on it.

None of the 17 patients was thought fit for discharge, and the only patient who was sent home after three courses of majeure, and in whom the "necessary" neurological side-effects appeared, broke up completely and had to return to this hospital after one week at home.

Based on these findings I do not consider that the dangers of this medication arise from a presumed individual sensitivity but from the intrinsic properties of the drug. These properties are clearly leading to many severe side-effects, which, to judge from my trial run, are in no proportion to therapeutic success, which should be the only yardstick for its exhibition.—I am, etc.,

St. Augustine's Hospital,
Chartham Down,
Nr. Canterbury, Kent.

R. H. V. OLLENDORFF.

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- ² Ollendorff, R. H. V., *Amer. J. Psychiat.*, 1960, **116**, 729.

Christmas Disease and Capillary Abnormality

SIR,—The cases of Christmas-factor deficiency associated with capillary anomalies reported by Dr. E. K. Blackburn and others (January 20, p. 154) and Dr. Katherine Dormandy and her colleagues (February 24, p. 566), as well as those previously described,¹⁻⁴ are of considerable importance in our understanding of the blood-clotting mechanism and its disorders. By indicating the presence of two types of factor-IX (Christmas-factor) deficiency, with and without capillary defect, analogous to von Willebrand's syndrome and true haemophilia respectively, these cases portray further the clinical and genetic similarities between factor-IX and factor-VIII (antihaemophilic-globulin) deficiencies.

In contrast, these two blood-clotting factors exhibit striking differences in their *in vitro* properties. Indeed, on these differences are based most of our diagnostic laboratory tests. This raises for consideration the possibility that, in collecting blood for routine blood-coagulation tests, some of the *in vivo* properties of either or both factors are altered. Recent investigations⁵ in this department by specially devised techniques proved this to be the case.—I am, etc.,

Department of Pathology,
Southmead Hospital,
Bristol.

F. NOUR-ELDIN.

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- ⁴ Nour-Eldin, F., *Thrombos. Diathes. haemorrh. (Stuttg.)*, 1960, **5**, 93.
- ⁵ Lewis, F. J. W., and Nour-Eldin, F., *Blood*, in press.

A Case of Breast Cancer

SIR,—During the interesting discussion on "A Case of Breast Cancer" (March 24, p. 857) the following remarks were made.

"Professor RUSSELL FRASER: The surgeon always tells you when the patient comes up with a history of one year what bad luck it is that she didn't come earlier; but in fact it is really a good sign, isn't it, that she will do well?"

"Professor DONIACH: Yes, I quite agree."

At first sight these remarks might suggest that there is no harm in delaying treatment for a year. That such an idea is quite absurd would be obvious to all those taking part in the discussion, but might be misunderstood by the casual reader. Of course it is "a good sign," first because she is still alive, and secondly because it means that she has a well-differentiated, slowly growing, late-disseminating type of tumour. Such cases do well whether treated by surgery or by radiotherapy.—I am, etc.,

Cancer Information Service,
Oxford.

MALCOLM DONALDSON.

Emigration of British Doctors

SIR,—It must now be clear to everyone except the purblind and euphoric Minister of Health that there really is an emigration of doctors on a large and unprecedented scale equivalent to one-third of the annual output of the medical schools, and that there is no escaping the conclusion that this disastrous exodus is mainly due to dissatisfaction with the N.H.S.

In the voluminous correspondence on the subject there are two points that have escaped notice. First, the